30–35 ml/min as stated in the present KDIGO clinical practice guidelines may be too low.

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The Authors Reply: For patients with chronic kidney disease stage 3 without evidence of bone or mineral disorder, the Kidney Disease Improving Global Outcomes workgroup recommended treatment for osteoporosis as in the general population. Over 80% of women with osteoporosis have chronic kidney disease stage 3 or 4 (ref. 1). Most of these elderly patients with age-related chronic kidney disease are not examined by nephrologists. In determining appropriate therapy for osteoporosis, the reduction in hip fracture and, potentially, in mortality, must be balanced against adverse events. In the pivotal trials of zoledronic acid, a transient increase in serum creatinine was noted in 1.3% of the patients on the drug and in 0.4% on placebo in 3889 osteoporotic patients.[2] In a study of 1065 patients with a recent hip fracture, an increase in serum creatinine was seen in 6.2% of patients on the drug and 5.6% on placebo. There was a 28% reduction in overall mortality with the drug.[3]

As Dr Woo has written, there are some newer reports of renal damage that have emerged from post-marketing surveillance.[4] However, the incidence of these adverse events is still low, 18 per 100,000 per year, and most of the patients had only a transient increase in creatinine. Thus, preventing the devastating consequences of a hip fracture will usually outweigh this small risk of kidney damage. To reduce the risk, physicians should follow guidelines about infusion rates, avoid volume depletion, or the administration of concomitant nephrotoxic medications. In addition, using oral dosing may help reduce this risk.

Once the kidney disease has progressed to chronic kidney disease–mineral and bone disorder (which is not determined by the estimated glomerular filtration rate but by abnormalities in calcium, phosphate, parathyroid hormone, or alkaline phosphatase), there is very little evidence about either safety or efficacy because these patients were excluded from the clinical trials. Therefore, we could not recommend the use of these drugs in the Kidney Disease Improving Global Outcomes guidelines. These patients must be treated on an individual basis, and we agree that the possibility of aggravated progression of renal disease should now be taken into consideration.

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Hypophosphatemia in patients with autosomal dominant polycystic kidney disease: the role of fibroblast growth factor 23 or loss of sodium/phosphate cotransporter?

To the Editor: We read with great interest the contribution by Pavik *et al.*[1] They reported increased fibroblast growth factor 23 (FGF23) and decreased serum phosphate levels in autosomal dominant polycystic kidney disease (ADPKD), and speculated the association between FGF23 and increased renal phosphate excretion. We would like to suggest another possible mechanism of hypophosphatemia in ADPKD patients.

According to an *in vivo* study by Vogel *et al.*,[2] the type II sodium/phosphate cotransporter (NaPi-2) in the brush border membrane (BBM) of proximal tubules has the central role of renal phosphate (Pi) absorption. During progression of ADPKD, the proximal nephron is damaged by the